

(12) **UK Patent Application** (19) **GB** (11) **2 333 705** (13) **A**

(43) Date of A Publication 04.08.1999

(21) Application No 9802071.2

(22) Date of Filing 31.01.1998

(71) Applicant(s)

**The Procter & Gamble Company**  
(Incorporated in USA - Ohio)  
One Procter & Gamble Plaza, Cincinnati, Ohio 45202,  
United States of America

(72) Inventor(s)

**Anthony Joseph Simpson**  
**Barry Stoddart**  
**Barry Thomas Ingram**  
**Stephen Wayne Heinzman**

(74) Agent and/or Address for Service

**Jillian Wendy Peet**  
**Procter & Gamble Technical Centres Ltd.**  
**Newcastle Technical Centre, P.O.Box Forest Hall No 2,**  
**NEWCASTLE UPON TYNE, NE12 9TS,**  
**United Kingdom**

(51) INT CL<sup>6</sup>

**A61K 31/195**

(52) UK CL (Edition Q )

**A5B BHA B170 B40Y B401 B41Y B411 B822**  
**U1S S1122 S1465**

(56) Documents Cited

**None**

(58) Field of Search

**UK CL (Edition P ) A5B BFG BHA**  
**INT CL<sup>6</sup> A61K**  
**Online: CAS ONLINE**

(54) Abstract Title

**Skin care compositions containing complexing agents (eg ethylenediamine disuccinic acid) for the treatment of skin rash arising from metal dermatitis**

(57) The invention relates the use of specific complexing agents (in particular ethylenediamine disuccinic acid, EDDS) for preparation of compositions, which can be applied to the skin to prevent or reduce or treat skin rash resulting from metal dermatitis. The invention also relates to specific cosmetic compositions, which will reduce or prevent skin rash. The invention also relates to the use of such a composition to prevent or reduce such a skin rash. The compositions can be applied to the skin or hair or to metal-containing products, which can be in close contact with the skin.

**GB 2 333 705 A**

5

### Skin Care Composition

- 10 The invention relates to compositions, which will reduce or prevent skin rash resulting from metal dermatitis.

### Background

15

- Skin rash caused by metal dermatitis has always been a problem encountered by people exposed to (high quantities of) certain metal ions. Exposure to nickel in the environment is widespread due to the frequent use of this metal in such everyday articles as studs, costume jewellery, wristwatches and clothing buckles. But it also has important occupational implications. Sensitisation to nickel, with the development of dermatitis, is an industrial hazard in certain occupations, e.g. electroplating, storage battery production, nickel refining and in certain chemical processes, including the production of glass or enamel. Dermatitis in these occupation may be persistent and result in loss of time from work. There is thus a need for these users to a solution to this type of skin rash problem.

25

- In the last decades, various creams have been developed which can serve as a protective barrier for the skin, thus reducing the exposure of the skin to the metal ions. Also, several substances that chemically bind nickel have been investigated for their ability to prevent the symptoms of nickel allergic contact dermatitis. These substances are usually incorporated into topical preparations, but oral treatments have also been used. Most of these treatments differ from conventional barrier creams in that the active constituents react with nickel and render it inactive.

30

- Also, metal-chelating materials have been investigated in nickel-sensitive individuals in an attempt to demonstrate a blocking effect on nickel dermatitis. The effect of EDTA for example has been shown to be attributable to reduced penetration of the nickel chelate into the epidermis of the skin or only to reduce binding of nickel to skin proteins, as for example discussed in 'Contact Dermatitis', 1995, 32, 100-106. The chelating or complexing agents forms a soluble, non-ionised stable chelate with nickel, making it chemically inactive.

40

- However, it has now been found that these complexing agents are not always effective complexing agents for those metal ions, which can cause dermatitis, such as nickel, cobalt and chromium, in particularly when other metal ions are present on the

45

skin or in the compositions. Thus, the traditionally used complexing agents have to be used in very high levels to perform, which in turn can be harmful to the user. Thus, there is still a need for improved methods to reduce the skin rash caused by metal dermatitis.

5 The inventors have found that certain complexing agents, in particular ethylene diamine disuccinic acid or EDDS, can very effectively bind the metal ions, which cause the metal dermatitis, in particular copper and nickel and particularly when other ions, such as calcium ions, are present. Since calcium ion concentrations are generally high on the surface of the skin or hair, the complexing agents of the invention will be more effective when applied to the skin or hair, than traditionally used complexing agents. Thus, it has been found that the use of these complexing agents in compositions, which can comprise high levels of calcium and which can be applied to the skin or hair, or the metal substances itself, prior to or during exposure of the skin or hair to the metals, results in a very effective reduction or a prevention of metal dermatitis, also when calcium ions are present in the compositions or on the skin. Furthermore, it has been found that even very small amounts of these complexing agents in these compositions can effectively give the required prevention or reduction of metal dermatitis.

### Summary of the Invention

25 The invention relates to the use of ethylene diamine disuccinic acid or a salt (EDDS) for preparation of a composition for treatment of metal dermatitis.

30 According to a preferred aspect of the invention, in use a source of calcium ions is also present in the composition. Hereby is meant that the calcium ions can be present in the composition containing the EDDS prior to use, and/ or in use, the calcium ion can become present in the compositions, e.g. by the application of the compositions to the skin, which contains calcium ions.

35 The invention also relates to compositions, which may be a cosmetic compositions, preferably in the form of a spray, cream, foam, lotion, gel, oil, ointment or powder, for treatment of metal dermatitis, comprising a complexing agent, which in use comprises calcium ions and one or more metal ions, selected from the group consisting of Cu, Fe, Zn, Ni, Co (herein referred to as 'the selected metal ions'), whereby the  $-\log_{10}C_T$  is equal to or greater than the smallest value of A or B, where

40 A is  $-\log_{10}(L_T \cdot M_T)$  and B is  $K_1(1 - K_2 \sqrt{I})(1 - K_3 \cdot \exp(-K_4 \cdot P))$ ,

$C_T$  is the total concentration of calcium ions,  $L_T$  is the total concentration of complexing agent,  $M_T$  is the total concentration of the metal ions, selected from the group consisting of Cu, Fe, Zn, Ni and Co; P is the pH of the composition, I is the

ionic strength of the composition, wherein all concentrations are in moles/ litre, where K1, K2, K3 and K4 are the following constants for the metals ions:

	Cu <sup>++</sup>	Fe <sup>++</sup>	Zn <sup>++</sup>	Ni <sup>++</sup>	Co <sup>++</sup>
K1	11.062	5.754	7.963	13.098	7.642
K2	0.496	0.479	0.619	0.535	0.652
K3	2.479	9385.0	24.202	1.473	32.069
K4	0.227	1.092	0.506	0.126	0.532

5

The invention also relates to the use of these compositions for the treatment of metal dermatitis, preferably nickel or copper dermatitis, in particular in the presence of calcium ions.

- 10 The cosmetic compositions can be in the form of a spray, cream, lotion, foam, oil, ointment, powder or gel.

#### Detailed Description of the Invention

15

##### Metal Dermatitis

- 20 The compositions of the invention are suitable for the treatment of dermatitis caused by metal ions present on the skin and other conditions which are associated with prolonged contact of the skin with metals or metal surfaces, or metal ions. By treatment is meant herein the prevention or reduction of the dermatitis or the rash of the skin which can result from the contact of the skin with specific metal ions, or at least stabilising the dermatitis or rash of the skin which can result from the contact of the skin with specific metal ions.

25

In particular, dermatitis caused by nickel, chromium or copper can be treated with the compositions of the invention.

- 30 It can be preferred that if one of the metal ions, causing the dermatitis, is nickel or copper, the composition has a pH of 4 or more.

##### pH Measurement

- 35 The pH as used herein can be determined by any known method of calculating or measuring the pH of an aqueous solution.

##### Ionic Strength Measurement

The ionic strength (I) can be determined by the following equation:

40

$$I = \frac{1}{2} \sum c_i z_i^2,$$

wherein  $c$  is the molecular concentration of the soluble ion (i) and  $z$  is the charge of the soluble ion (i).

5

### Complexing Agent

10 In one embodiment, the invention provides ethylene diamine disuccinic acid or salts thereof, for preparation of a composition for treatment, prevention or reduction of metal dermatitis.

15 The invention also relates to complexing agents, which in the presents of calcium ions, selectively binds the metal ions which cause the dermatitis. These complexing agents are such that a cosmetic compositions is obtained, as described above.

A highly preferred complexing agent for use in aqueous compositions of the invention is N, N ethylene diamine disuccinic acid or its salt (EDDS).

20 It is known that the (S,S) EDDS isomer is more readily biodegradable than the (R,R) isomer. Thus, depending of the application of the aqueous compositions of the invention, it may be desirable to use only one of the isomers of EDDS. It may be preferred that a racemic mixture of the isomers is used in the aqueous compositions, for example because the racemic mixture is less expensive.

25

The exact level of incorporation of the complexing agents in the compositions of the invention will depend on the nature of the compositions and the mode of applications. However, in general even small amounts of complexing agents can be sufficient to obtain the required prevention or reduction of dermatitis. Typical  
30 amount of complexing agnets can be from 0.001% by weight to 30% by weight, more preferably from 0.005% to 10%, more preferably from 001% to 5% by weight of the composition..

35

### Method of Preparation of the Compositions

The compositions can be prepared by any method known in the art for preparation for cosmetic compositions. The exact method will depend on the nature of the composition. The complexing agent can be added to the compositions in its acid or salt form, or be combined with other ingredients commonly used in cosmetic  
40 compositions, or dispersed or dissolved in water or oil or a water-in-oil emulsion prior to addition to the composition.

### Method of use of Compositions

The composition of the invention can be applied directly to the skin or hair, which will be in contact with, or the vicinity of the metals or metal ions., which can be  
 5 topically applied to the skin.

The compositions can also be applied (firstly) to an article, such as a wipe or tissue, which will then be applied to the skin.

10 The compositions of the invention can also be applied to a metal surface, which will be brought in the vicinity or contact with the skin or hair.

The required, effective amount of the composition will vary with the particular location of the condition being treated, the severity of the condition being treated, the  
 15 expected duration of the treatment, any specific sensitivity to either the composition itself, or the concentration of the complexing agent to the user, the condition of the user, concurrent therapies being administered, other conditions present in the user.

### 20 Additional Ingredients

The composition of the invention can comprise additional ingredients. Which ingredients are present and at which level depends on the character of the composition and the use thereof. Thus for example lotions will generally comprise  
 25 different additional ingredients to powders.

It can be preferred that the compositions comprise one or more other ingredient which can reduce the metal dermatitis. Preferred can be the use of certain polymeric compounds, such as a polyoxyethylene-polyoxypropylene copolymer (Pluronic® gel),  
 30 polyethylene glycols, polyurethanes, synthetic carbopol polymers, compounds which can help the healing of the skin, such as vitamins (vitamin E) and cortisone's, and also compounds to soften the skin such as vaseline, glycerin, triethyleneglycol, lanolin, paraffin and another group of polymers extensively employed by pharmaceutical and cosmetic manufactures, as also described herein.

35 Depending on the application of the compositions of the invention, a preferred additional ingredient can be one or more builders or dispersants. It can be preferred that a crystal growth inhibitor is present, preferably in addition to dispersants.

40 Suitable examples of water-soluble phosphates, suitable as crystal growth inhibitors or builders, are the alkali metal tripolyphosphates, sodium, potassium and ammonium pyrophosphate, sodium and potassium and ammonium pyrophosphate, sodium and potassium orthophosphate, sodium polymeta/phosphate in which the degree of polymerization ranges from about 6 to 21, and salts of phytic acid.

45

Any builder or dispersant material known in the art can be used. Particularly useful builders or dispersants can be monomeric, oligomeric and polycarboxylate-containing components, polymeric components, borate-containing components and phosphate-containing components and silicate and aluminosilicate-containing components.

Suitable polycarboxylates or polycarboxylic acids can be succinic acid, malonic acid, (ethylenedioxy) diacetic acid, maleic acid, diglycolic acid, tartaric acid, tartronic acid and fumaric acid; citrates, aconitrates and citraconates as well as succinate derivatives such as the carboxymethyloxysuccinates described in British Patent No. 1,379,241, lactoxysuccinates described in British Patent No. 1,389,732, and aminosuccinates described in Netherlands Application 7205873, and the oxypolycarboxylate materials such as 2-oxa-1,1,3-propane tricarboxylates described in British Patent No. 1,387,447; oxydisuccinates disclosed in British Patent No. 1,261,829, 1,1,2,2-ethane tetracarboxylates, 1,1,3,3-propane tetracarboxylates and 1,1,2,3-propane tetracarboxylates; sulfosuccinate derivatives disclosed in British Patent Nos. 1,398,421 and 1,398,422 and in U.S. Patent No. 3,936,448, and the sulfonated pyrolysed citrates described in British Patent No. 1,439,000;

Polymeric components include the water soluble organic homo- or co-polymeric polycarboxylic acids or their salts in which the polycarboxylic acid comprises at least two carboxyl radicals separated from each other by not more than two carbon atoms. Polymers of the latter type are disclosed in GB-A-1,596,756. Examples of such salts are polyacrylates of MWt 1000-5000 and their copolymers with maleic anhydride, such copolymers having a molecular weight of from 2000 to 100,000, especially 40,000 to 80,000.

The polyamino components are useful herein including those derived from aspartic acid such as those disclosed in EP-A-305282, EP-A-305283 and EP-A-351629.

Terpolymers containing monomer units selected from maleic acid, acrylic acid, polyaspartic acid and vinyl alcohol, particularly those having an average molecular weight of from 5,000 to 10,000, are also suitable herein.

Other polymeric components suitable for incorporation in the compositions herein include cellulose derivatives such as methylcellulose, carboxymethylcellulose, hydroxypropylmethylcellulose and hydroxyethylcellulose.

Further useful polymeric components are the polyethylene glycols, particularly those of molecular weight 1000-10000, more particularly 2000 to 8000 and most preferably about 4000.

Other preferred ingredients are amorphous or crystalline, preferably layered, silicate or aluminosilicate materials or builders. Suitable aluminosilicate zeolites have the unit cell formula  $\text{Na}_z[(\text{AlO}_2)_z(\text{SiO}_2)_y] \cdot x\text{H}_2\text{O}$  wherein  $z$  and  $y$  are at least 6; the molar

ratio of z to y is from 1.0 to 0.5 and x is at least 5, preferably from 7.5 to 276, more preferably from 10 to 264. The aluminosilicate materials are in hydrated form and are preferably crystalline, containing from 10% to 28%, more preferably from 18% to 22% water in bound form.

5

#### Lotions, Creams, Oils, Foams, Ointments, Gels, Powders and the Like

The present compositions can be used for any suitable purpose. In particular, the present compositions are suitable for topical application to the skin or hair. In particular, the skin care compositions can be in the form of creams, lotions, gels, and the like. Preferably the cosmetic compositions herein are in the form of an oil-in-water emulsion of one or more oil phases in an aqueous continuous phase, each oil phase comprising a single oily component or a mixture of oily components in miscible or homogeneous form but said different oil phases containing different materials or combinations of materials from each other. The overall level of oil phase components in the compositions of the invention is preferably from about 0.1% to about 60%, preferably from about 1% to about 30% and more preferably from about 1% to about 10% by weight.

The present compositions preferably comprise, as either all or a portion of the oil phase or oil phases referred to above a first silicone-containing phase comprising a crosslinked polyorganosiloxane polymer and a silicone oil, wherein the composition comprises 0.1% to about 20%, preferably from about 0.5% to about 10%, more preferably from about 0.5% to about 5%, by weight of composition, of the combination of crosslinked silicone and silicone oil.

Compositions herein preferably also comprise a second non-crosslinked silicone-containing phase. In preferred embodiments the second silicone-containing phase is present in a level of from about 0.1% to about 20%, especially from about 0.1% to about 10% by weight of composition.

Suitable silicone fluids for use in the second silicone-containing phase herein include water-insoluble silicones inclusive of non-volatile polyalkyl and polyaryl siloxane gums and fluids, volatile cyclic and linear polyalkylsiloxanes, polyalkoxylated silicones, amino and quaternary ammonium modified silicones, and mixtures thereof.

In preferred embodiments the second silicone-containing phase comprises a silicone gum or a mixture of silicones including the silicone gum. As used herein, the term "silicone gum" means high molecular weight silicone-based fluids having a mass-average molecular weight in excess of about 200,000 and preferably from about 200,000 to about 400,000. Silicone oils generally have a molecular weight of less than about 200,000. Typically, silicone gums have a viscosity at 25°C in excess of about 1,000,000 mm<sup>2</sup>.s<sup>-1</sup>. The silicone gums include dimethicones as described by Petrarch and others including US-A-4,152,416, May 1, 1979 to Spitzer, et al, and Noll, Walter, Chemistry and Technology of Silicones, New York:



Academic Press 1968. Also describing silicone gums are General Electric Silicone Rubber Product Data Sheets SE 30, SE 33, SE 54 and SE 76.

5 In preferred embodiments, another, third, oil phase is present in an amount of from about 0.1% to about 15%, more preferably from about 1% to about 10% by weight of composition. The third oil phase can be either a separate phase or can form one phase together with either or both of the first and second silicone phases. Preferably, the third oil phase is a separate phase.

10 This oil phase preferably comprises a non-silicone organic oil, such as a natural or synthetic oil selected from mineral, vegetable, and animal oils, fats and waxes, fatty acid esters, fatty alcohols, fatty acids and mixtures thereof, which ingredients are useful for achieving emollient cosmetic properties.

15 Suitable first oil phase components for use herein include, for example, optionally hydroxy-substituted C<sub>8</sub>-C<sub>50</sub> unsaturated fatty acids and esters thereof, beeswax, saturated and unsaturated fatty alcohols such as behenyl alcohol and cetyl alcohol, hydrocarbons such as mineral oils, petrolatum and squalane, fatty sorbitan esters (see US-A-3988255, Seiden, issued October 26 1976), lanolin and lanolin derivatives, animal and vegetable triglycerides  
20 such as almond oil, peanut oil, wheat germ oil, linseed oil, jojoba oil, oil of apricot pits, walnuts, palm nuts, pistachio nuts, sesame seeds, rapeseed, cade oil, corn oil, peach pit oil, poppyseed oil, pine oil, castor oil, soybean oil, avocado oil, safflower oil, coconut oil, hazelnut oil, olive oil, grapeseed oil, shea butter, shorea butter, and sunflower seed oil and C<sub>1</sub>-C<sub>24</sub> esters of dimer and trimer acids such as diisopropyl dimerate, diisostearylmalate,  
25 diisostearyldimerate and triisostearyltrimerate. Of the above, highly preferred are the mineral oils, petrolatums, unsaturated fatty acids and esters thereof and mixtures thereof.

#### Amphiphilic Surfactant

30 A further preferred component of the compositions herein is an organic amphiphilic surfactant which is capable of forming smectic lyotropic crystals in product or when the product is being applied to the skin at ambient or elevated temperatures. Preferably the amphiphilic surfactant is capable of forming liquid crystals at a temperature in the range from about 20°C to about 40°C. Preferably the amphiphilic  
35 surfactant is capable of forming smectic lyotropic liquid crystals. Once application of the product to the skin has been completed, liquid crystals may not be identifiable on the skin surface or stratum corneum. The amphiphilic surfactant is preferably present at a level of from about 0.1% to about 20%, preferably from about 0.1% to about 10%, by weight.

40 Organic amphiphilic surfactants suitable for use herein include those having a weight average HLB (Hydrophilic Lipophilic Balance) in the range from about 2 to about 12, preferably from about 4 to about 8.

Preferred organic amphiphilic surfactants employed herein have a long saturated or unsaturated branched or linear lipophilic chain having from about 12 to about 30 carbon atoms such as oleic, lanolic, tetradecylic, hexadecylic, isostearyl, lauric, coconut, stearic or alkyl phenyl chains. When the hydrophilic group of the amphiphilic material forming the liquid crystal phase is a nonionic group, a polyoxyethylene, a polyglycerol, a polyol ester, oxyalkylated or not, and, for example, a polyoxyalkylated sorbitol or sugar ester, can be employed. When the hydrophilic group of the amphiphilic surfactant forming the liquid crystal phase is an ionic group, advantageously there can be used, as the hydrophilic group, a phosphatidylcholine residue as found in lecithin.

The compositions can also comprise Amphoteric, anionic, nonoionic and cationic surfactants.

A wide variety of optional ingredients such as non-occlusive moisturizers, humectants, gelling agents, neutralizing agents, perfumes, colouring agents and surfactants, can be added to the skin compositions herein.

The compositions herein can comprise a humectant. Suitable humectants for use herein include sorbitol, propylene glycol, butylene glycol, hexylene glycol, ethoxylated glucose derivatives, hexanetriol, glycerine, glycine, hyaluronic acid, arginine, Ajidew (NaPCA), water-soluble polyglycerylmethacrylate lubricants and panthenols. A preferred humectant herein is glycerine (sometimes known as glycerol or glycerin). Chemically, glycerine is 1,2,3-propanetriol and is a product of commerce. One large source of the material is in the manufacture of soap. Glycerine is especially preferred in the compositions of the invention from the viewpoint of boosting moisturisation. Also preferred for use herein is butylene glycol. Particularly preferred from the viewpoint of boosting moisturisation is a combination of glycerine and urea.

In the present compositions, the humectant is preferably present at a level of from about 0.1% to about 20%, more preferably from about 1% to about 15%, and especially from about 5% to about 15% by weight of composition.

The compositions of the invention can also contain a hydrophilic gelling agent at a level preferably from about 0.01% to about 10%, more preferably from about 0.02% to about 2%, and especially from about 0.02% to about 0.5%. The gelling agent preferably has a viscosity (1% aqueous solution, 20°C, Brookfield RVT) of at least about 4000 mPa.s, more preferably at least about 10,000 mPa.s and especially at least 50,000 mPa.s.

Suitable hydrophilic gelling agents can generally be described as water-soluble or colloiddally water-soluble polymers, and include cellulose ethers (e.g. hydroxyethyl cellulose, methyl cellulose, hydroxypropylmethyl cellulose), polyvinylpyrrolidone, polyvinylalcohol, guar gum, hydroxypropyl guar gum and xanthan gum.

Preferred hydrophilic gelling agents herein, however, are acrylic acid/ethyl acrylate copolymers and the carboxyvinyl polymers sold by the B.F. Goodrich Company under the trade mark of Carbopol resins. These resins consist essentially of a colloiddally water-soluble polyalkenyl polyether crosslinked polymer of acrylic acid crosslinked with from 0.75% to 2.00% of a crosslinking agent such as for example polyallyl sucrose or polyallyl pentaerythritol. Examples include Carbopol 934, Carbopol 940, Carbopol 950, Carbopol 954, Carbopol 980, Carbopol 951 and Carbopol 981. Carbopol 934 is a water-soluble polymer of acrylic acid crosslinked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. A most preferred polymer is Carbopol 954. Also suitable for use herein are hydrophobically-modified cross-linked polymers of acrylic acid having amphipathic properties available under the Trade Name Carbopol 1382, Carbopol 1342 and Pemulen TR-1 (CTFA Designation: Acrylates/10-30 Alkyl Acrylate Crosspolymer). A combination of the polyalkenyl polyether cross-linked acrylic acid polymer and the hydrophobically modified cross-linked acrylic acid polymer is also suitable and is preferred for use herein. The gelling agents herein are particularly valuable for providing excellent stability characteristics over both normal and elevated temperatures.

Neutralizing agents suitable for use in neutralizing acidic group containing hydrophilic gelling agents herein include sodium hydroxide, potassium hydroxide, ammonium hydroxide, monoethanolamine, diethanolamine and triethanolamine.

Other optional materials include keratolytic agents/desquamation agents such as salicylic acid; proteins and polypeptides and derivatives thereof; water-soluble or solubilizable preservatives preferably at a level of from about 0.1% to about 5%, such as Germall 115, methyl, ethyl, propyl and butyl esters of hydroxybenzoic acid, benzyl alcohol, EDTA, Euxyl (RTM) K400, Bronopol (2-bromo-2-nitropropane-1,3-diol) and phenoxypropanol; antibacterials such as Irgasan (RTM) and phenoxyethanol (preferably at levels of from 0.1% to about 5%); soluble or colloiddally-soluble moisturising agents such as hylaronic acid and starch-grafted sodium polyacrylates such as Sanwet (RTM) IM-1000, IM-1500 and IM-2500 available from Celanese Superabsorbent Materials, Portsmouth, VA, USA and described in USA-A-4,076,663; vitamins such as vitamin A, vitamin C, vitamin E and vitamin K; alpha and beta hydroxyacids; aloe vera; sphingosines and phytosphingosines, cholesterol; skin whitening agents; N-acetyl cysteine; colouring agents; perfumes and perfume solubilizers and additional surfactants/emulsifiers such as fatty alcohol ethoxylates, ethoxylated polyol fatty acid esters, wherein the polyol can be selected from glycerine, propyleneglycol, ethyleneglycol, sorbitol, sorbitan, polypropyleneglycol, glucose and sucrose. Examples include glyceryl monohydroxy stearate and stearyl alcohol ethoxylated with an average of from 10 to 200 moles of ethylene oxide per mole of alcohol and PEG-6 caprylic/capric glycerides.

The compositions of the present invention can also comprise a safe and effective amount of vitamins, such as vitamin E, B, preferably vitamin B<sub>3</sub> vitamin A or retinoid. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1% to about 10%, even more

preferably from about 0.5% to about 10%, and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the vitamin.

5 The pH of the compositions is preferably from about 4 to about 9, more preferably from about 6 to about 8.0.

10 The balance of the composition is water or an aqueous carrier suitable for topical application to the skin. The water content of the compositions herein is generally from about 30% to about 98.89%, preferably from about 50% to about 95% and especially from about 60% to about 90% by weight.

The compositions of the invention are preferably in the form of a moisturising cream or lotion, which can be applied to the skin as a leave-on product.

The invention is illustrated by the following examples

### Examples 1-3

Oil-in-water emulsions are prepared from the following ingredients using  
5 conventional formulating techniques.

	Ex 1	Ex 2	Ex 3
Cetyl Alcohol	0.72	0.72	0.72
Stearyl Alcohol	0.48	0.48	0.48
Stearic Acid	0.1	0.1	0.1
PEG-100 Stearate	0.1	0.1	0.1
Arlatone 2121	1	1	1
Silicone Q21403	2	2	2
Fatty acid ester of sugar <sup>1</sup>	0.67	0.67	0.67
Glycerin	7	7	7
Urea	2	0	0
Carbopol 954	0.68	0.5	0.5
Carbopol 1382	0.1	0.1	0.1
TiO <sub>2</sub>	0.75	0.75	0.75
Glydant Plus	0.1	0.1	0.1
S,S EDDS	0.1	0.1	0.1
distilled water	qs 100	qs 100	qs 100

<sup>1</sup> A C1-C30 monoester or polyester of sugars and one or more carboxylic acid  
moieties as described herein, preferably a sucrose polyester in which the degree of  
esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-  
10 unsaturated and behenic, in a molar ratio of unsaturates:behenic of 1:7 to 3:5, more  
preferably the octaester of sucrose in which there are about 7 behenic fatty acid  
moieties and about 1 oleic acid moiety in the molecule, e.g., sucrose ester of  
cottonseed oil fatty acids, e.g., SEFA Cottonate.

### 15 Preparation:

A first premix of thickening agents, glycerine/TiO<sub>2</sub> premix, Arlatone 2121 and other  
water soluble ingredients apart from urea, is prepared by admixing in water and  
heating to about 80°C. A second premix of the oil phase ingredients including the  
emulsifiers, oil-soluble preservatives, other than silicone gum is prepared by mixing  
20 and heating and is added to the aqueous premix.

The resulting mixture is cooled to about 60°C. The EDDS, silicone gum, and then  
urea solution (1g dissolved in 1ml of water) are then added to the resulting oil-in-  
water emulsion and the mixture is cooled before adding minor ingredients. The  
25 composition is ready for packaging.

### Claims

1. Use of a ethylene diamine disuccinic acid or salts thereof (EDDS) for preparation of a composition for treatment of metal dermatitis.
2. Use according to claim 1, wherein the metal dermatitis is nickel and/ or copper dermatitis.
3. Use of a composition according to claim 1 or 2 for treatment of metal dermatitis, in the presence of calcium ions.
4. A cosmetic composition for treatment, prevention or reduction of metal dermatitis, comprising a complexing agent, and in use comprising calcium ions and one or more metal ions, selected from the group consisting of Cu, Fe, Zn, Ni, Co, whereby the  $-\log_{10}C_T$  is equal to or greater than the smallest value of A or B, wherein

$$A \text{ is } -\log_{10}(L_T \cdot M_T) \text{ and } B \text{ is } K_1(1 - K_2 \sqrt{I})(1 - K_3 \cdot \exp(-K_4 \cdot P)),$$

$C_T$  is the total concentration of calcium ions,  $L_T$  is the total concentration of complexing agent,  $M_T$  is the total concentration of the metal ions, selected from the group consisting of Cu, Fe, Zn, Ni and Co; P is the pH of the composition, I is the ionic strength of the composition, wherein all concentrations are in moles/litre, where  $K_1$ ,  $K_2$ ,  $K_3$  and  $K_4$  are the following constants for the metals ions:

	Cu <sup>++</sup>	Fe <sup>+++</sup>	Zn <sup>++</sup>	Ni <sup>++</sup>	Co <sup>++</sup>
K1	11.062	5.754	7.963	13.098	7.642
K2	0.496	0.479	0.619	0.535	0.652
K3	2.479	9385.0	24.202	1.473	32.069
K4	0.227	1.092	0.506	0.126	0.532

5. A cosmetic composition according to claim 4, being an aqueous composition, obtainable by a process comprising the step of addition of the complexing agent to an aqueous solution, comprising calcium ions and the metal ions selected from the consisting of Cu, Fe, Zn, Ni, Co.
6. A cosmetic composition according to claim 4 or 5, wherein the complexing agent is EDDS, present at a level of from 0.001% to 30% by weight of the composition.
7. A cosmetic composition according to any of claims 4 to 6, wherein the metal ions are nickel and/ or copper.

8. A composition according to Claims 7 wherein the composition is in the form of an emulsion, preferably an oil-in-water emulsion.
  9. Use of a composition according to any of claims 4 to 8 for treatment of metal dermatitis in the presence of calcium ions.
- 5



The  
**Patent  
Office**  
15

**Application No:** GB 9802071.2  
**Claims searched:** 1-9

**Examiner:** Stephen Quick  
**Date of search:** 27 April 1998

**Patents Act 1977**  
**Search Report under Section 17**

**Databases searched:**

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.P): A5B (BFG, BHA)

Int Cl (Ed.6): A61K

Other: Online: CAS ONLINE

**Documents considered to be relevant:**

Category	Identity of document and relevant passage	Relevant to claims
	No documents of relevance found	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.